Oxygen uptake before and after the onset of claudication during a 6-minute walk test

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Objective: **This study compared oxygen uptake before and after the onset of claudication in individuals with peripheral artery disease (PAD) during a 6-minute walk test, and identified predictors of the change in oxygen uptake after the onset of claudication pain.**

Methods: **The study included 50 individuals with PAD. During a 6-minute walk test, 33 experienced claudication (pain group), and 17 were pain-free (pain-free group). Oxygen uptake and ambulatory cadence were the primary outcomes evaluated during the 6-minute walk test.**

Results: **The pain group experienced onset of claudication pain at a mean (standard deviation) of 179 (45) meters and continued to walk to achieve a 6-minute walk distance of 393 (74) meters, which was similar to the 401 (76) meters walked in the pain-free group ($P = .74$). Oxygen uptake increased ($P < .0001$) after the onset of pain in the pain group, and this change was greater ($P = .025$) than the increase in oxygen uptake from the second to fifth minutes of walking in the pain-free group. Ambulatory cadence decreased after the onset of pain in the pain group ($P = .0003$). The change in oxygen uptake was associated with metabolic syndrome ($P = .0023$), 6-minute walk distance ($P = .0037$), age ($P = .0041$), and oxygen uptake during the second minute of the test ($P = .012$).**

Conclusion: **Claudication increases oxygen uptake of self-paced, over-the-ground ambulation, despite a decrease in cadence. The pain-mediated increase in oxygen uptake was blunted in individuals with metabolic syndrome, suggesting that the ability to increase oxygen uptake during ambulation is impaired. The clinical significance is that claudication increases the metabolic cost of ambulation, thereby increasing the relative intensity of exercise and reducing the tolerance to sustain ambulation. (J Vasc Surg 2011;54:1366-73.)**

Peripheral artery disease (PAD) is prevalent in >12% of the U.S. population aged ≥65 years[1] and is associated with elevated rates of mortality[2-5] and morbidity,[6] because >60% of these individuals have concomitant cardiovascular or cerebrovascular disease, or both.[7] In addition, many of those with PAD are physically limited by ambulatory leg pain. Claudication is prevalent in >6% of those aged ≥65 years,[1,7] which results in impaired ambulation,[8,9] reduced physical function,[10,11] and lower daily physical activity.[12]

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This research was supported by grants from the National Institute on Aging (R01-AG-24296) to Dr Gardner, by an Oklahoma Center for the Advancement of Science and Technology grant (HR04-113S) to Dr Gardner, and by the University of Oklahoma Health Sciences Center General Clinical Research Center grant (M01-RR-14467), sponsored by the National Center for Research Resources from the National Institutes of Health.

Competition of interest: none.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a competition of interest.

0741-5214/$36.00

doi:10.1016/j.jvs.2011.04.026

Less is known about how the onset of claudication acutely affects ambulation. Oxygen uptake is increased with the onset of claudication during treadmill exercise at constant load, thereby increasing the relative metabolic cost of painful ambulation and reducing exercise tolerance.[13] Whether the increase in oxygen uptake after pain onset during treadmill walking is evident during self-paced, over-the-ground ambulation is not clear because individuals may compensate by slowing their pace[14,15] to maintain a given metabolic cost. However, slowing freely-chosen velocity by too much results in less economic ambulation,[16-18] which may increase oxygen uptake even further during painful ambulation. The oxygen uptake of self-paced, over-the-ground ambulation during pain-free and painful ambulation, which has not been previously examined, has important implications regarding the intensity at which ambulation is performed in the community setting.

This study compared oxygen uptake before and after the onset of claudication in individuals with PAD during a 6-minute walk test (6-MWT), and identified predictors of the change in oxygen uptake after the onset of claudication pain. We hypothesized that oxygen uptake would increase after the onset of claudication and that the severity of PAD and the change in ambulatory cadence and velocity would predict the change in oxygen uptake after the onset of claudication.

METHODS

The procedures used in this study were approved by the Institutional Review Board at the University of Oklahoma

Health Sciences Center (UOHSC). Written informed consent was obtained from each participant before the investigation.

Participant recruitment. Study participants were evaluated in the General Clinical Research Center at the UOHSC. Participants were recruited by referrals from the HSC Vascular Clinic and by newspaper advertisements for possible enrollment into a randomized controlled exercise rehabilitation study.[19] The data and analyses for this study were part of the baseline assessments obtained for the exercise study.

Screening. Individuals with claudication secondary to vascular insufficiency were included in this study if they had (1) a history of any type of exertional leg pain, (2) ambulation during a graded treadmill test limited by leg pain consistent with claudication,[8] and (3) an ankle-brachial index (ABI) ≤0.90 at rest[1,7] or an ABI ≤0.73 after exercise, because some PAD patients have normal values at rest which only become abnormal after an exercise test.[20] Exclusion criteria were:

1. Absence of PAD (ABI >0.90 at rest and ABI >0.73 after exercise);
2. Inability to obtain an ABI measure due to noncompressible vessels;
3. Asymptomatic PAD (Fontaine stage I) determined from the medical history and verified during the graded treadmill test;
4. Use of medications indicated for the treatment of claudication (cilostazol and pentoxifylline) initiated ≤3 months before the investigation;
5. Exercise tolerance during maximal treadmill exercise limited by factors other than claudication pain, such as severe coronary artery disease, dyspnea, and poorly controlled blood pressure;
6. Active cancer, end-stage renal disease, or liver disease;
7. Discontinuing ambulation for any reason during the 6-MWT; and
8. For those experiencing pain during the 6-MWT, ambulating for <1 complete minute during pain-free or painful conditions because an insufficient amount of data was available for analyses.

The study evaluated 77 individuals, and 50 were deemed eligible. Demographic information, height, weight, body mass index (BMI), waist and hip circumferences,[21] cardiovascular risk factors, comorbid conditions, claudication history, blood samples, and a list of current medications were obtained from a medical history and physical examination at the beginning of the study.

Measurements. Primary outcome measures were oxygen uptake and ambulatory cadence obtained during the 6-MWT.

Procedures. A trained technician administered the over-the-ground, 6-MWT in which two cones were placed 100 feet apart in a marked corridor, as previously described.[22] Participants were instructed to walk as many laps around the cones as possible while wearing a light-weight (0.8-kg) portable oxygen uptake unit (COSMED K4 b^2, COSMED USA, Inc, Chicago, Ill), which continuously measured oxygen uptake via indirect calorimetry. Participants also wore a step activity monitor (Step Watch 3, Cyma Inc, Mountlake Terrace, Wash) on their right ankle.

During the test, participants indicated if and when they experienced the onset of claudication pain. Those who experienced pain during the 6-MWT (pain group) were compared with those who completed the test without pain (pain-free group), as described subsequently in the Results.

Primary outcome measures

The 6-MWT was the experimental protocol used to obtain the primary outcome measures of oxygen uptake and ambulatory cadence, and other measures consisting of stride length, ambulatory velocity, time and distance to onset of pain, and total 6-minute walk distance (6-MWD). Oxygen uptake and ambulatory cadence were obtained each minute during the test, and the technician recorded the time and distance to onset of claudication and the total distance walked. Walking distances were converted from feet to meters.

Oxygen uptake and ambulatory cadence. These values obtained during the first and last minute of exercise in either group were not used for analyses because of the possibility that data were not recorded for a full 60 seconds during these time points. In the pain group, oxygen uptake and ambulatory cadence obtained during the minute in which the onset of claudication occurred was not used for analyses because it was not possible to precisely separate the data before and after the onset of pain within the minute.

Stride length and ambulatory velocity. These values were calculated in the pain group during pain-free and painful ambulation. However, these calculations were not possible to determine during the test in the pain-free group because (1) the participants did not experience claudication, and therefore, ambulation did not occur under painful conditions; and (2) time and distance measures were not recorded at specified intervals because of concerns that this additional encumbrance on the technician while the test was proceeding might affect the results of the self-paced 6MWT. Therefore, the calculation of stride length and ambulatory velocity at different times during the test in the pain-free group was not possible.

Change scores for oxygen uptake and gait parameters were calculated as the difference in average values obtained during painful ambulation minus the values obtained during pain-free ambulation in the pain group, and as the difference between the values at 5 minutes minus the values at 2 minutes during exercise in the pain-free group.

Secondary outcome measures

Walking Impairment Questionnaire. Self-reported ambulatory ability was obtained using the Walking Impairment Questionnaire (WIQ), which has been validated for PAD patients, that assesses ability to walk at various speeds and distances, and to climb stairs.[23]

Claudication times and peak oxygen uptake during graded treadmill test. Participants performed a progressive, graded treadmill protocol to determine study eligibility and to obtain outcome measures related to exercise performance.[8] The claudication onset time, defined as the walking time at which the individual first experienced pain, and the peak walking time, defined as the walking time at which ambulation could not continue due to maximal pain, were both recorded to quantify the severity of claudication. Peak oxygen uptake was measured by oxygen uptake obtained during the peak exercise workload with a Medical Graphics VO2000 metabolic system (Medical Graphics Inc, St Paul, Minn). The test–retest intraclass reliability coefficient for these methods is $R = .89$ for claudication onset time,[8] $R = .93$ for peak walking time,[8] and $R = .88$ for peak oxygen uptake.[24]

ABI and ischemic window. As previously described, ABI measures were obtained from the more severely diseased leg before and 1, 3, 5, and 7 minutes after the treadmill test.[8,25] The reduction in ankle systolic blood pressure after treadmill exercise from the resting baseline value was quantified by calculating the area under the curve, referred to as the ischemic window.[26] Because the ischemic window is a function of both PAD severity and the amount of exercise performed, the ischemic window was normalized per meter walked.

Ambulatory activity monitoring. Daily ambulatory activity was assessed using a step activity monitor, as previously described.[27] Ambulatory activity was measured during 7 consecutive days in which participants were instructed to wear the monitor during waking hours and to remove it before retiring to bed. The step activity monitor was attached to the right ankle above the lateral malleolus using elastic Velcro straps and continuously recorded the number of steps taken minute-to-minute. The accuracy of the step activity monitor exceeds 99% ± 1% in individuals with claudication.[27]

Statistical analyses. An independent sample *t* test was used to compare the means of continuous demographic and clinical measures between the pain group and the pain-free group. A χ^2 test, or Fisher exact test for small, expected data cell counts, was used to compare the distribution of categoric demographic and clinical measures between the two groups.

To address the first aim, a non-parametric Wilcoxon signed rank test was used to compare the median oxygen uptake measures and the median ambulatory parameters (cadence, speed, and stride length) between pain-free and painful ambulation in the pain group and between minutes 2 and 5 in the pain-free group. An independent sample Wilcoxon rank sum test was used for between-group comparisons of the distribution of changes in oxygen uptake and ambulatory parameters. For the pain-free time during the 6-MWT, between-group comparisons of mean values to a fixed reference were made using a one-sample *t* test. A two-sided $\alpha = 0.05$ was used to define statistical significance.

Table I. Clinical characteristics of study participants

Variable	*Pain group (n = 33) Mean (SD)*	*Pain-free group (n = 17) Mean (SD)*	P
Age, years	65 (9)	67 (11)	.59
Weight, kg	89.6 (18.7)	78.0 (17.4)	.038
Height, cm	171.0 (9.7)	169.2 (9.1)	.51
Body mass index, kg/m^2	30.6 (5.8)	27.6 (7.6)	.12
Waist girth, cm[a]	105.1 (16.0)	102.6 (18.2)	.74
Ankle/brachial index	0.72 (0.20)	0.75 (0.21)	.61
	Percentage	*Percentage*	
Sex, men	67	59	.58
White race	61	47	.36
Current smoking	36	35	.94
Diabetes	36	41	.74
Hypertension	88	76	.42
Hyperlipidemia	76	82	.73
Abdominal obesity[a]	63	71	>.99
Obesity	48	29	.20
Metabolic syndrome	88	65	.070

SD, Standard deviation.
[a]This measurement included 19 in the pain group and 7 in the pain-free group.

To address the second aim, linear regression was used to identify clinical and exercise performance characteristics that were independently associated with oxygen uptake after adjustment for height. Clinical and exercise performance characteristics associated with oxygen uptake univariately at an $\alpha = 0.05$ level were entered into a multiple linear regression model. Clinical and exercise performance characteristics were deleted from the multiple regression model until all terms were significant at the $\alpha = 0.05$ level. The clinical and exercise performance characteristics that were considered in the modeling are listed in Table I and Table II. Height was adjusted for in the regression model to adjust for the association between height and stride rate. Data were analyzed using SAS 9.1 software (SAS Institute Inc, Cary, NC) and SPSS 15.0 software (SPSS Inc, Chicago, Ill).

RESULTS

Participants were grouped according to whether they did (pain group; $n = 33$) or did not (pain-free group; $n = 17$) experience claudication during the 6-MWT. The groups were similar on all clinical characteristics ($P > .05$), except that the pain group had higher body weight ($P = .038$) and a nonsignificant trend for a higher prevalence of metabolic syndrome ($P = .070$; Table I). The groups were similar on all measures of treadmill exercise performance, WIQ measures, and daily ambulatory activity ($P > .05$; Table II), but the pain group, by definition, had shorter 6-minute walk pain-free time ($P < .001$) and pain-free distance ($P < .001$) than the pain-free group (Table III).

Oxygen uptake during pain-free ambulation increased ($P < .0001$) after the onset of pain in the pain group, and this change was greater ($P = .025$) than the increase in

Table II. Treadmill exercise performance, Walking Impairment Questionnaire measures, and daily ambulatory activity of participants

Variable	*Pain group (n = 33) Mean (SD)*	*Pain-free group (n = 17) Mean (SD)*	P
Claudication onset time, seconds	240 (178)	265 (214)	.68
Peak walking time, seconds	475 (194)	438 (212)	.55
Peak oxygen uptake, mL/kg/minute	13.5 (3.5)	12.6 (3.1)	.40
Ischemic window, mm Hg × minute/m	0.52 (0.45)	0.47 (0.62)	.74
Walking Impairment Questionnaire			
Distance score, %	39 (30)	45 (35)	.56
Speed score, %	35 (20)	42 (25)	.30
Stair climbing score %	45 (29)	42 (31)	.73
Daily ambulatory activity, strides/day	3719 (1811)	3688 (1920)	.96

SD, Standard deviation.

Table III. Six-minute walk test (*6-MWT*) measurements of participants

6-MWT variables	*Pain group (n = 33) Mean (SD)*	*Pain-free group (n = 17) Mean (SD)*	P
Pain-free time, seconds	156 (29)	360 (0)	<.0001[a]
Pain-free distance, m	179 (45)	401 (76)	<.0001
Walk distance, m	393 (74)	401 (76)	.74

SD, Standard deviation.
[a]Comparison made between 6-MWT pain-free time in the pain group and a fixed value of 360 seconds in the pain-free group using a one-sample *t* test.

oxygen uptake from minutes 2 to 5 of walking in the pain-free group (Fig 1, Table IV). In contrast, the decrease in ambulatory cadence after pain onset in the pain group ($P = .0003$) was similar ($P = .79$) to the decline in cadence from minutes 2 to 5 of walking in the pain-free group (Table IV). After pain onset, the pain group also experienced a shorter stride length ($P < .0001$), a decline in ambulatory velocity ($P < .0001$), and increased oxygen uptake when expressed per stride taken ($P < .0001$) or meter walked ($P < .0001$) than before pain onset (Table IV).

The multiple regression model predicting the change in oxygen uptake after the onset of claudication in patients in the pain group is presented in Table V. Metabolic syndrome was negatively associated with the increase in oxygen uptake after pain onset, because individuals with metabolic syndrome had on average a 1.83 mL/kg/min lower change in oxygen uptake than those without metabolic syndrome (Fig 2). In contrast, age, 6-MWD, and the oxygen uptake during the second minute of the 6-MWT were positively associated with the pain-mediated increase in oxygen uptake.

DISCUSSION

Changes in oxygen uptake and ambulatory cadence during painful ambulation. The primary finding was that oxygen uptake increased by 36% after the transition from pain-free to painful ambulation during the 6-MWT. This observation supports a previous report from our laboratory that that oxygen uptake was higher while ambulating with pain during a constant-speed, standardized treadmill test.[13] Whether the observed pain-mediated increase in oxygen uptake during treadmill exercise would occur during self-paced, over-the-ground ambulation was not clear because individuals can attempt to compensate by slowing their pace.

We found that ambulatory cadence decreased during painful ambulation, supporting previous reports of changes in gait measures after the onset of claudication, such as reduced ambulatory velocity,[15] shortened step length,[15] and decreased ankle plantar flexor moments[14] at self-selected pace over short distances. However, the reduction in ambulatory cadence during painful ambulation in the present study did not reduce the metabolic cost of walking.

Although this study does not address mechanisms for the increase in oxygen uptake during painful ambulation, it indicates that a given exercise work rate becomes more challenging to perform than pain-free ambulation. Muscle force production decreases with claudication,[28,29] which may explain the decrease in stride length during painful ambulation in the pain group. It is possible that the decrease in stride length during the test was greater in the pain group than in the pain-free group, and this may be one reason why the increase in oxygen uptake was not different between the two groups when expressed per stride taken.

When muscle force production decreases with claudication, the recruitment of more motor units per muscle is needed to generate the required force to ambulate.[18] A change in muscle fiber recruitment patterns would be consistent with more challenging ambulation,[18] suggesting that more motor units—particularly more fast-twitch motor units, which are less economical than slow-twitch fibers[30]—are recruited to perform painful ambulation. Furthermore, the muscle denervation observed in PAD participants[31] may impair optimal motor unit recruitment during exercise, becoming more evident during painful ambulation.

Those who completed the 6-MWT pain-free also had an increase in oxygen uptake during exercise, but the increase was smaller than the increase in those who per-

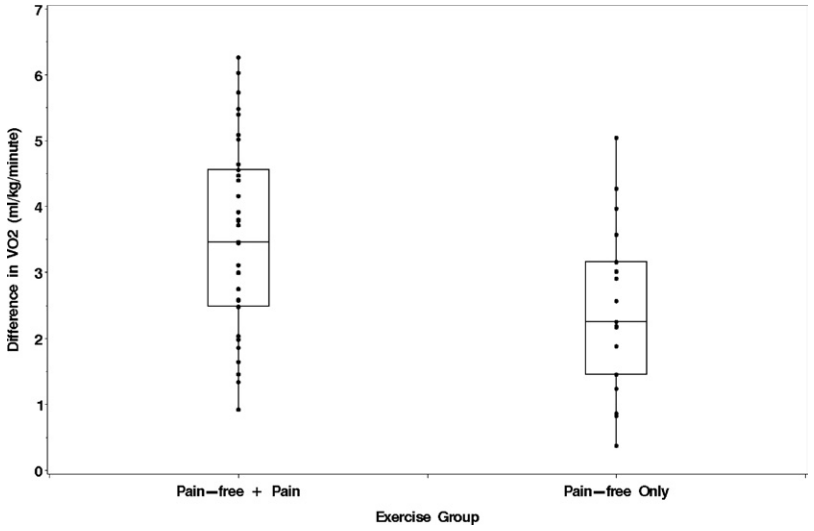

Fig 1. Box and whisker plots show the change in oxygen uptake (VO_2) during a 6-minute walk test in the pain group (n = 33) and the pain-free group (n = 17). The change in the pain group was defined as the VO_2 measured during painful ambulation minus the VO_2 during pain-free ambulation. The change in the pain-free group was defined as the VO_2 measured during the fifth minute minus the VO_2 measured during the second minute. The *horizontal line* in the middle of each box indicates the median; the *top* and *bottom borders* of the box mark the 75th and 25th percentiles, respectively; and the *whiskers* mark the minimum and maximum. The *dots* represent the observed data points.

Table IV. Oxygen uptake (VO_2) and gait measures during a 6-minute walk test in the pain-group (n = 33) and pain-free group (n = 17)

Variables[a]	*Time 1*[b]	*Time 2*[c]	*Change (time 2 − time 1)*	P *Change score*	*Difference between scores*
VO_2, mL/kg					
Per minute					
Pain group	8.4 (6.6 to 9.6)	11.4 (10.1 to 14.0)	3.5 (2.5 to 4.6)	<.0001	.025
Pain-free group	8.4 (7.5 to 10.2)	11.0 (10.2 to 12.6)	2.3 (1.5 to 3.2)	<.0001	
Per meter walked					
Pain group	0.10 (0.08 to 0.12)	0.14 (0.12 to 0.18)	0.05 (0.02 to 0.07)	<.0001	. . .
Pain-free group	. . .	. . .	. . .	. . .	
Per stride taken					
Pain group	0.18 (0.15 to 0.20)	0.21 (0.19 to 0.26)	0.04 (0.02 to 0.06)	<.0001	.36
Pain-free group	0.17 (0.13 to 0.20)	0.21 (0.19 to 0.26)	0.05 (0.03 to 0.07)	<.0001	
Velocity, m/minute					
Pain group	66.6 (61.8 to 75.5)	65.9 (53.5 to 69.2)	−4.4 (−13.3 to −1.7)	<.0001	. . .
Pain-free group	. . .	. . .	. . .	. . .	
Cadence, strides/minute					
Pain group	55.0 (52.0 to 56.0)	54.0 (50.5 to 56.0)	−1.0 (−1.5 to 0.0)	.0003	.79
Pain-free group	53.0 (50.0 to 56.0)	52.0 (50.0 to 54.0)	0.0 (−1.0 to 0.0)	.0078	
Stride length, m/stride					
Pain group	1.25 (1.13 to 1.39)	1.17 (1.09 to 1.33)	−0.05 (−0.14 to −0.02)	<.0001	. . .
Pain-free group	. . .	. . .	. . .	. . .	

[a]Data summaries are median (interquartile range: 25th-75th percentiles).
[b]Values during time 1 were obtained during pain-free ambulation in the pain group and during the second minute of ambulation in the pain-free group.
[c]Values for time 2 were obtained during painful ambulation in the pain group and during the fifth minute of ambulation in the pain-free group.

formed painful ambulation. A gradual increase in oxygen uptake has been observed during intense exercise compared with light exercise, thus preventing oxygen uptake from reaching a steady-state plateau during exercise at a constant workload.[32] Because the pain-free group ambulated at a relatively high intensity equal to 72% of their peak oxygen uptake during the second minute of exercise, it is not surprising that they experienced a gradual increase in oxygen uptake, referred to as the slow component of the increase in oxygen uptake, which we have previously ob-

Table V. Multiple regression model predicting the change in oxygen uptake (VO_2) after the onset of claudication in the 33 individuals in the pain group

Variables				
Dependent	*Independent*	*Regression coefficient*	*95% CI*	P
ΔVO_2[b]	Age, years	0.064	0.022 to 0.11	.0041
	Metabolic syndrome[a]	−1.83	−2.93 to −0.71	.0023
	6-MWD, total meters	0.0093	0.0033 to 0.015	.0037
	Minute 2 VO_2[b]	0.20	0.049 to 0.36	.012
	Height, cm	−0.014	−0.061 to 0.033	.54

6-MWD, 6-minute walk distance; *CI,* confidence interval
[a]No syndrome reference.
[b]Calculated as mL/kg/min.

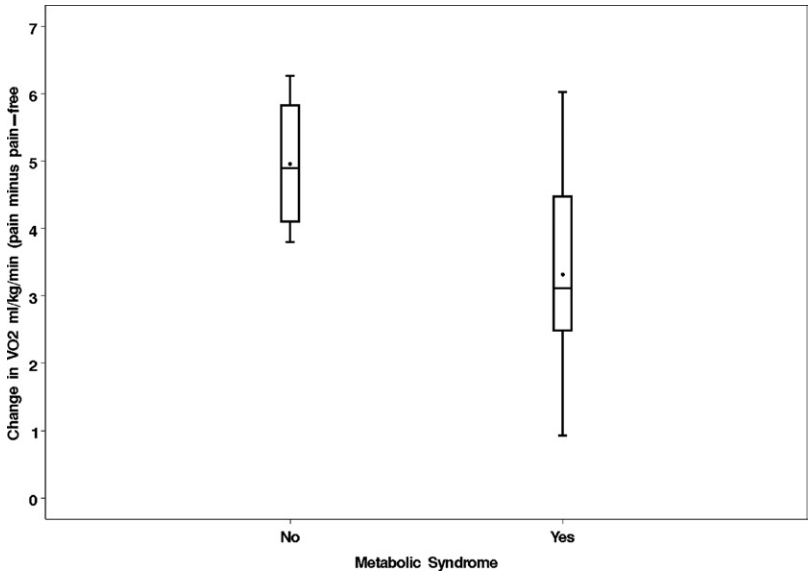

Fig 2. Box and whisker plots show the change in oxygen uptake (VO_2) during a 6-minute walk test in participants with and without metabolic syndrome in the pain group. The change in VO_2 was defined as the value measured during painful ambulation minus the value obtained during pain-free ambulation. The *horizontal line* in the middle of each box indicates the median; the *top* and *bottom borders* of the box mark the 75th and 25th percentiles, respectively; and the *whiskers* mark the minimum and maximum. The *dot* in the middle of each box indicates the mean.

served in PAD individuals walking on a treadmill at a constant work rate.[33]

Our data show a lack of agreement between the claudication onset time and peak walking time obtained during a standardized treadmill test and the pain-free time and distance obtained during the 6-MWT. Although 33 individuals experienced claudication during the 6-MWT, and therefore had shorter pain-free walking time and distance than the 17 participants who did not experience claudication, there were no group differences in claudication onset time and peak walking time values during treadmill exercise. This supports our previous finding that there is no significant correlation between the pain-free distance during the 6-MWT and the claudication onset time and peak walking time obtained during a standardized treadmill test.[22] This suggests that the two tests measure different aspects of ambulatory function in individuals with PAD and claudication.

The average, freely chosen walking speed during the 6-MWT was ~2.5 mph, which was higher than the 2.0-mph speed during the treadmill test; thus, the 6-MWT was performed at a higher exercise intensity during the first few minutes than the treadmill test, and it is not surprising that two-thirds of the participants (ie, pain group) experienced claudication sooner during the 6-MWT than during the treadmill test. However, it is surprising that one-third of the participants (ie, pain-free group) did not experience claudication during the 6-MWT, even though they walked at a faster pace than during the treadmill test.

Although both groups attempted to walk as fast as they could during the 6-MWT, it is possible that individuals in the pain-free group walked closer to their optimal speed

during the 6-MWT and that the walking speed during the treadmill test was relatively too slow for them. When expressed as per distance traveled, walking too slow is equally inefficient as walking too fast, thereby decreasing efficiency.[17] Thus, the faster pace during the 6-MWT may have been more comfortable for the pain-free group than the slower pace during the treadmill test, even though a 2% incline was added after the first 2 minutes of the treadmill test.

Predictors of the pain-mediated change in oxygen uptake. Oxygen uptake increased after the onset of claudication in individuals ambulating during a 6-MWT. Metabolic syndrome was a predictor of the pain-mediated change in oxygen uptake. This finding suggests that insulin resistance may interfere with central and peripheral factors affecting the kinetics of oxygen uptake. For example, type 2 diabetes slows whole-body oxygen uptake kinetics and heart rate kinetics during exercise,[34] slows oxidative enzyme activity,[35] increases the frequency of mitochondrial DNA deletions in skeletal muscle,[36] impairs endothelial function,[37] reduces leg blood flow during steady-state exercise,[38] and slows microvascular blood flow kinetics.[39] Data from our laboratory also support these findings: reactive hyperemic calf blood flow is blunted in PAD patients with metabolic syndrome compared with those without metabolic syndrome, and they have more limited 6-MW performance.[40]

Additional factors predictive of the change in pain-mediated oxygen uptake were age, 6-MWD, and the oxygen uptake during the second minute of the test. The increase in oxygen uptake was greater in older individuals, in those who maintained a fast pace during the test even after pain onset to achieve a longer total distance, and in those who had high oxygen uptake values during the early phase of the test.

Limitations. This study has several limitations. The regression coefficients calculated between oxygen uptake and clinical characteristics and baseline exercise performance measures from this cross-sectional design do not allow causality to be established. The present findings are also limited by the relatively small sample sizes, particularly in the pain-free group.

Potential group differences in comorbid conditions were not included in this study, such as arthritis, chronic obstructive pulmonary disease, and congestive heart failure, which may partially explain the group difference in the change in oxygen uptake during the 6-MW. However, these comorbid conditions would be of minimal importance unless the prevalence of these conditions was different between groups. Furthermore, the effect of these conditions (eg, arthritic pain) would typically be present throughout the entire walking test, thereby not eliciting an increase in oxygen uptake at any particular point during the test like we found for the onset of claudication.

In addition, this study is limited to PAD participants who have claudication, and may not be generalized to individuals with less severe or more severe PAD. However, the participants in the current study are typical of those with claudication, because there was a good proportion of women and African Americans, and a high prevalence of cardiovascular risk factors for PAD, including smoking, diabetes, hypertension, dyslipidemia, and obesity. Thus, the findings of the present study appear generalizable to individuals with claudication who typically have numerous comorbid conditions.

CONCLUSIONS

Claudication increases oxygen uptake of self-paced, over-the-ground ambulation, despite a decrease in cadence. The pain-mediated increase in oxygen uptake was blunted in participants with metabolic syndrome, suggesting that they have an impaired ability to increase oxygen uptake during ambulation. The clinical significance is that claudication increases the metabolic cost of ambulation, thereby increasing the relative intensity of exercise and reducing the tolerance to sustain ambulation. This information is clinically relevant to exercise professionals who rehabilitate patients with PAD, because the training intensity should be reduced to compensate for the expected increase in intensity during painful ambulation, thereby providing a safer and more effective exercise prescription. A long-term goal is to determine whether the efficacy of interventions designed to improve claudication translates to improved self-paced, over-the-ground ambulation, evident by delayed occurrence of pain and by attenuation of the increase in oxygen uptake, as individuals transition from pain-free to painful ambulation.

AUTHOR CONTRIBUTIONS

Conception and design: AG, RRD, PM
Analysis and interpretation: AG, JS
Data collection: AK, SB
Writing the article: AG
Critical revision of the article: AG, RRD, JS, PM, AK, SB
Final approval of the article: AG, RRD, JS, PM, AK, SB
Statistical analysis: JS
Obtained funding: AG

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Submitted Feb 23, 2011; accepted Apr 12, 2011.